Remarks

I. Status of the Claims

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-5, 9, 12-18, 20-21 and 24-32 and 34-39 are pending in the application, with 1, 12, 14-16, 27, 28 and 34 being the independent claims. Claims 1-5, 9, 12-18, 20, 21, 24-27, and 34-39 have been withdrawn. Claims 28 and 32 are sought to be amended. Claim 33 has been canceled without prejudice or disclaimer. Applicants reserve the right to file one or more continuation applications directed to the subject matter of the canceled claims.

II. The Amendments

Claims 34-39 have been withdrawn in view of the Restriction Requirement and the Examiner's comments in the previous Office Action.

Claim 33 has been canceled as requested by the Examiner.

Claim 28 has been amended to recite that the protein having 90% identity to galectin-3 is a protective diabetes-mediating protein. Support for this amendment can be found, *inter alia*, in the specification at page 17, lines 8-15.

Claim 32 has been amended to include the correct spelling of the term "diabetes mellitus."

These changes are believed to introduce no new matter and their prompt entry is respectfully requested.

III. The Objection to the Claims

At page 3 of the Office Action, the Examiner has objected to claim 33 under 37 C.F.R. § 1.75 on the ground that "it is a substantial duplicate of claim 32 because it is well-known that insulin dependent diabetes mellitus (melitis) is type I diabetes. Without acquiescing in the propriety of the rejection, and solely in the interests of expediting prosecution, Applicants have canceled claim 33. Accordingly, the ground for the objection has been obviated and the objection may be withdrawn.

IV. The Rejections

A. The Written Description Rejection

At page 3 of the Office Action, the Examiner has rejected claims 28-39 under 35 U.S.C. § 112, first paragraph, on the ground that the specification does not reasonably convey to one of ordinary skill in the art that Applicants had possession of claimed subject matter at the time the application was filed. Specifically, the Examiner contends that Applicants are not in possession of methods of treating diabetes with proteins having 90-95% sequence identity to galectin-3, and suggests that Applicants amend the claims to include an assayable function. Applicants respectfully traverse the rejection.

Without acquiescing in the propriety of the rejection, and solely in the interests of expediting prosecution, Applicants have amended claim 28 to require that the protein that has 90-95% sequence identity with human galectin-3 is "protective diabetes-mediating protein." As amended, the claims encompass a very specific group of proteins that all share a common function (*i.e.*, they are all protective diabetes-mediating proteins) as well as a common structural relationship (*i.e.*, homology to human galectin-3). The

specification describes with particularity what constitutes a protective diabetes-mediating protein, as well as assays for identifying and isolating such protective diabetes-mediating proteins. (Application at page 17, lines 8-15, and pages 24-26.)

Accordingly, Applicants are in possession of the necessary common attributes possessed by members of the claimed genus of protective diabetes-mediating proteins. Reconsideration and withdrawal of the rejection are, therefore, respectfully requested.

B. The Enablement Rejection

At page 4 of the Office Action, the Examiner has rejected claims 28-39 under 35 U.S.C. § 112, first paragraph, on the ground that they encompass subject matter which is not described in the specification in a way as to enable one skilled in the art to make and/or use the invention. In particular, the Examiner suggests that the putative role of galectin-3 in treating or preventing diabetes is based on Applicants' determination that galectin-3 is down-regulated at the onset of IDDM. The Examiner contends, however, that: "The art teaches that down-regulation of a protein does not necessarily correlate with a potential of said protein being used for treating or preventing diabetes." The Examiner cites the relationship between TNF-α expression and diabetes as an example. As a result, the Examiner concludes that: "The specification at best suggests that galectin-3 expression regulation occurs when diabetes develops, but [does] not adequately disclose how to prevent said diabetes using the claimed composition." Applicants respectfully traverse the rejection.

At the outset, Applicants point out that there is a presumption that the claims are enabled, and that the burden is on the Examiner to provide evidence demonstrating a clear

lack of enablement. In the present case, the sole basis set forth by the Examiner for the rejection appears to be the Examiner's belief that Applicants identified galectin-3 as a therapeutic candidate for preventing/treating diabetes based *only* on the fact that the it's expression is down-regulated during diabetes. However, this is incorrect.

In fact, the specification does contain specific teachings regarding the protective effect of galectin-3 in treating diabetes. For example, the application teaches not only that galectin-3 expression was significantly *down-regulated* at day 7 and at disease-onset in diabetes-prone BB rats, an accepted animal model of insulin-dependent diabetes mellitus in humans, but also that galectin-3 expression was *increased* in *in vitro* IL-1β stimulated islets and in grafts from animals *which did not develop disease*. *See* Example 8. Thus, the "putative role" for galectin-3 in diabetes is based not only on the fact that it is down-regulated at disease onset, but also because expression is increased in disease-resistant rats.

In addition, the specification further describes the expression of galectin-3 in RIN cells, a cultured line of insulinoma cells. The present inventors found that RIN cells expressing gal-3 exhibited an *increased metabolic activity and proliferative rate* and became *more resistant to the negative effect of cytokines* such as IL-1 β. (*See* page 39, lines 4-9; and page 1, lines 10-21.) The Examiner previously acknowledged that IL-1β is a primary mediator of the diabetes disease state. (*See* Office Action of June 17, 2003, at 12.) Taken together, these data are strong evidence that galectin-3 is a protective diabetes-mediating protein capable of preventing or ameliorating symptoms of diabetes in humans.

Several subsequent references support the correlation between galectin-3 and diabetes identified by Applicants. For example, Pugliese *et al.* (whose findings were previously cited by the Examiner in support of the rejection) conducted experiments that demonstrated that "galectin-3 deficiency resulted in accelerated diabetic glomerulopathy."

In particular, the authors concluded: "[t]his finding was associated with marked renal/glomerular AGE [advanced glycosylation end products] accumulation and a modified expression pattern of the other AGE receptors linked to the genotype, suggesting that it was attributable to the lack of galectin-3 AGE receptor function." (Pugliese *et al.*, *FASEB J. 15*:2471-2479 (2001) at page 2478.) (Exhibit A). In another study, Iacobini *et al.* determined that AGE play a pivotol role in modulating target tissue injury in diabetes, and that "galectin-3 acts as an AGE receptor to *protect* from AGE-induced tissue injury." (*See* Iacobini *et al.*, *J. Am. Soc. Nephrol. 14*:S264-S270 (2003)) (Exhibit B).

In view of the Examiner's mistaken understanding of the teachings of the specification, and further in view of the post-filing date evidence supporting Applicants' claimed therapeutic use of galectin-3, Applicants respectfully submit that the Examiner has not met the requisite burden of showing that the claims lack enablement, and the rejection should be withdrawn.

C. The Rejection Under 35 U.S.C.§ 112, Second Paragraph

At page 5 of the Office Action, that Examiner has rejected claim 32 under 35 U.S.C. § 112, second paragraph, as being indefinite due to a misspelling of the term "diabetes mellitus." Applicants respectfully traverse the rejection.

Without acquiescing in the propriety of the rejection, and solely in the interests of expediting prosecution, Applicants have amended claim 32 to correct the misspelling. Accordingly, the ground for the rejection has been obviated and the rejection may be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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